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Modelling the cost-effectiveness of anti-TNFs for the treatment of psoriatic arthritis

David Epstein, Laura Bojke, Mark Sculpher, Dawn Craig, Mark Rodgers, Nerys Woolacott and Yang Huiquin

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Project objectives

- To determine the clinical effectiveness, safety and cost-effectiveness of etanercept, infliximab and adalimumab for the treatment of active and progressive PsA in patients who have an inadequate response to standard treatment (including DMARD therapy).
- Deliverables:
  - Review of clinical evidence
  - Synthesis of clinical evidence
  - Review of cost-effectiveness literature
  - **De –novo cost-effectiveness model**

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Updates from a previous York model

- Incorporate the biologic adalimumab (only etanercept and infliximab compared to palliative care in previous model).
- Incorporate the effect of biologics on psoriasis aspect of disease (measure using the PASI).
- Incorporate any additional trials.
- Update parameters of the model, including: withdrawal rates, elicited evidence on rebound, costs of disease and natural history data.

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Decision model

- Probabilistic lifetime (40 years) cohort model implemented in R (previously implemented in Excel).
- The model aims to be consistent with licensed indications and current BSR and BAD guidelines for the use of biologics in PsA.
- The parameters of the model were obtained from published literature, manufacturers' parameter estimates, evidence synthesis and a structured elicitation of expert opinion.
- Patients have PsA with mild-to-moderate psoriasis in the base-case. Sub-groups are also presented.

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Model structure

- Initial response to treatment determined using PSARC and PASI-75. Base-case assumes those with PSARC response at 3 months will continue on biologic drug.
- Associated HAQ and PASI scores.
- After first 3 months, no subsequent change in HAQ or PASI while remaining on biologic.
- Assume constant rate of withdrawal from biologics after 3 months. In the base-case, patients will return to palliative care, with rebound equal to initial gain.
- HAQ steadily deteriorates with palliative care.
- Costs of treatment and related to HAQ and PASI score
- HAQ and PASI mapped onto utilities.

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Model figure

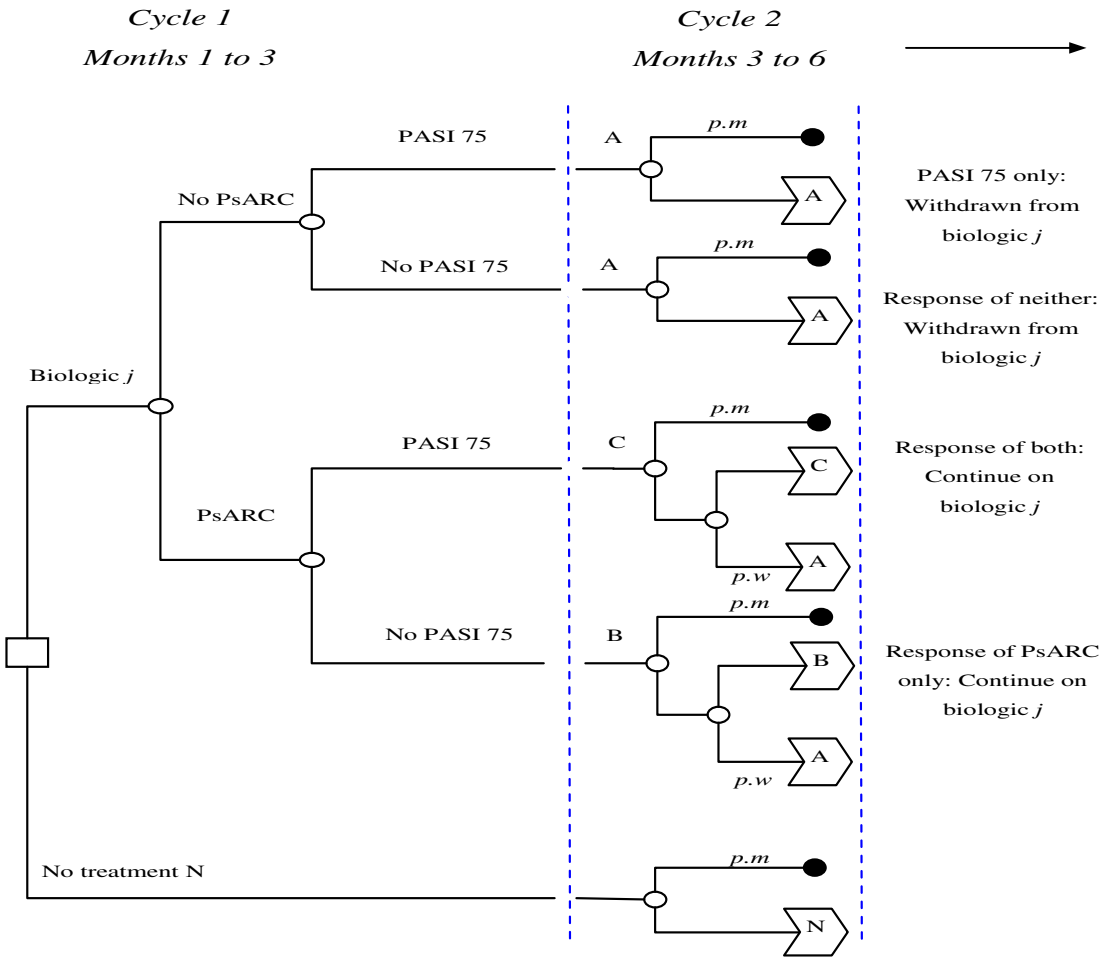

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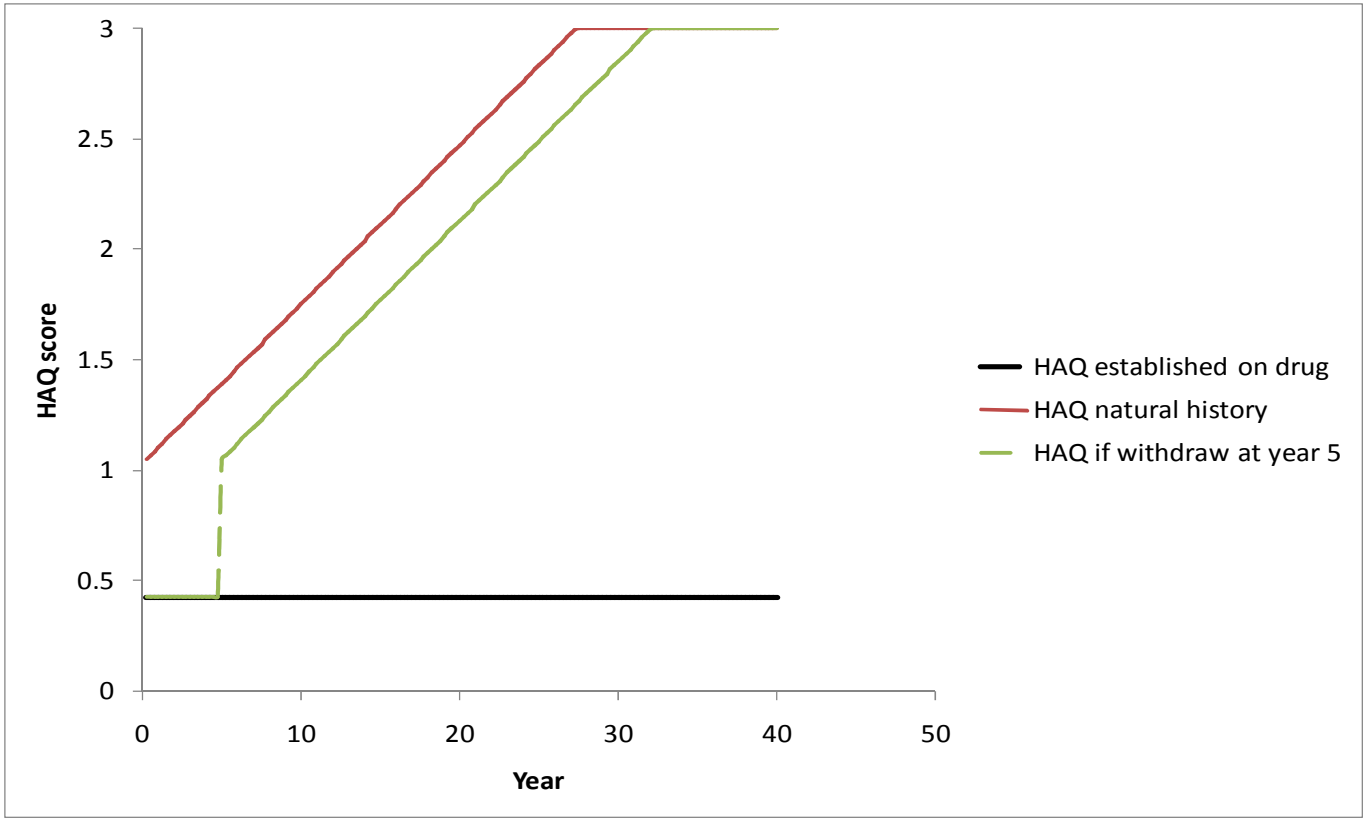
Illustration of the progression of arthritis



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Evidence synthesis

- Relative efficacy between the alternative biologics determined using Bayesian indirect comparison methods.
- The evidence synthesis provided the following parameters for the decision model (by drug & for placebo):
  - Probability of PSARC response
  - Probability of PASI response
  - Associated HAQ for PSARC responder/non responder
- We estimated the probability of PSARC response only, PASI response only, both PSARC and PASI response, or neither response, using data from a RCT on the correlation between the 2 types of responses.

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Some specific issues

- Expected improvement in PASI for PASI 75 responders
  - Response indicators (PASI 50, 75 and 90) indicate the probability of achieving a *minimum* percentage improvement in PASI compared with baseline. Decision model requires the *mean* absolute or percentage change in PASI. It was assumed that those achieving PASI 75 (but not PASI 90) have a 75% mean improvement and those achieving PASI 90 have a 90% mean improvement
  - Can explore the consequences of using alternative decision rules about whether to withdraw biologic therapy, e.g. withdraw only if fail to achieve both PsARC and PASI 75 response
- Rates of withdrawal
  - Registry data synthesised using method for meta-analysis at multiple follow up times

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Specific issues (2)

- Adjustments made for the possible placebo/expectancy effects
  - Predicting the absolute effectiveness of biologics in general practice. Would we get similar absolute response rates we see in RCTs, or does the RCT setting induce a ‘placebo effect’?
  - Affects the comparison between biologics and ‘active therapy’, palliative care.
- Maintenance of initial improvement in HAQ
  - Elicitation exercise designed to generate estimates of progression after initial gain and effect of withdrawal from biologics on HAQ.
  - Synthesised results used to inform uncertainty around HAQ rebound following withdrawal.

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Results: base-case

Strategy	QALY	Cost £	Inc QALY	Inc cost	ICER	PCE 20K	PCE 30K
N	5.241	42205				0.414	0.282
A	6.642	66408	1.401	24202	Ex dom	0.044	0.020
E	7.115	72172	0.473	5763	15986	0.524	0.566
I	7.430	89107	0.315	16935	53750	0.018	0.132

- For patients with PsA and mild-to-moderate skin disease, the ICER etanercept versus palliative care is ~ £16,000 per QALY
- The ICER of infliximab versus etanercept is ~ £54,000 per QALY. Adalimumab is extendedly dominated.

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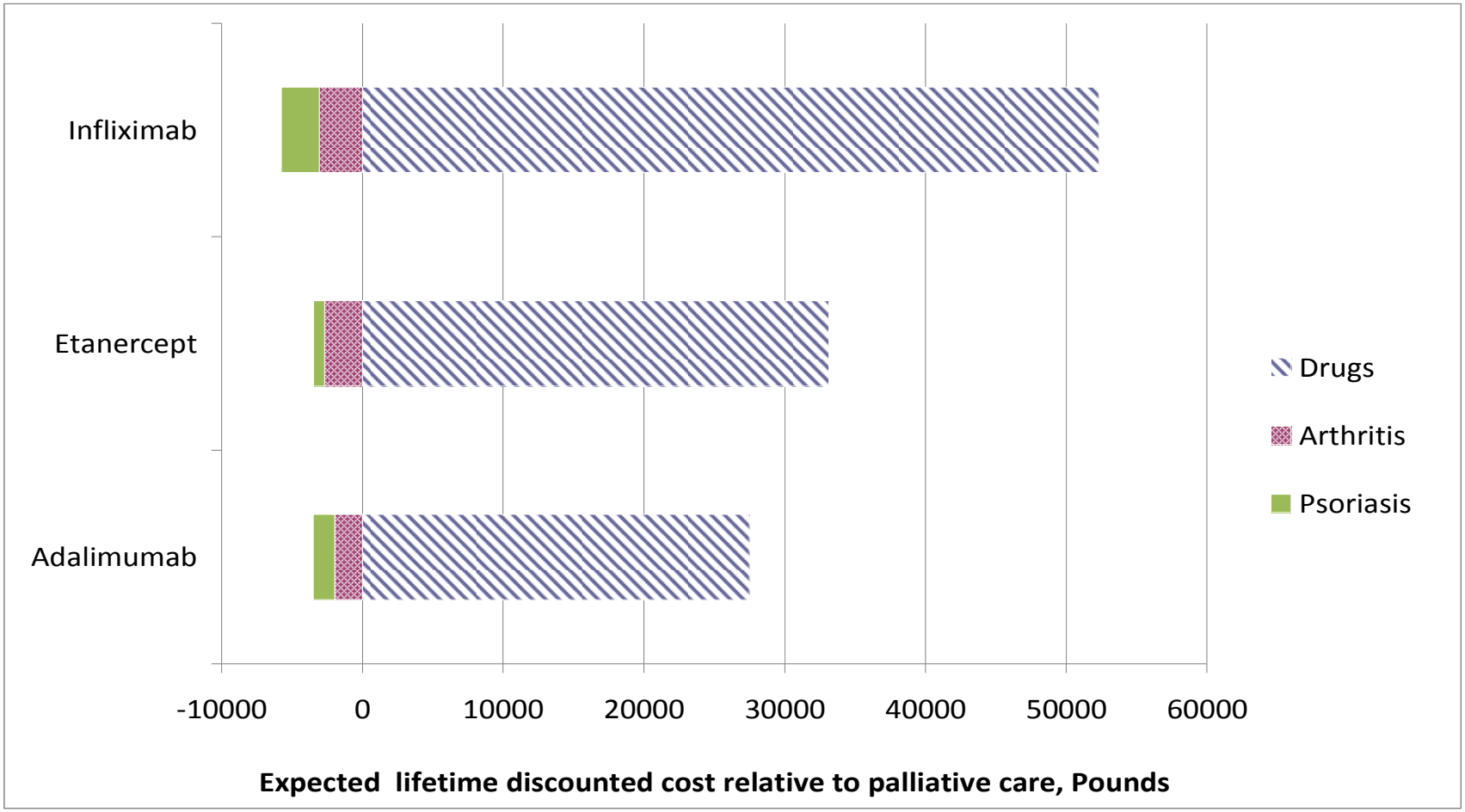
Lifetime discounted costs of PsA

- Lifetime discounted costs of biologic drugs, and cost savings for arthritis and psoriasis, relative to non-biologic treatments for PsA



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Gains in lifetime discounted QALYs

- Gains in lifetime discounted QALYs associated with treating arthritis and psoriasis in PsA with biologic therapies, relative to palliative care

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Results: subgroups

- For patients with PsA and moderate-to-severe skin disease, the ICER of adalimumab versus palliative care is ~ £15,000 per QALY.
- The ICER of etanercept versus adalimumab is ~ £16,000 per QALY and the ICER for infliximab versus etanercept is ~t £36,000 per QALY.
- Etanercept has the greatest probability (0.432) of being cost-effective at a £20,000 threshold.
- For patients with PsA with negligible skin involvement, the ICER of etanercept versus palliative care is ~ £17,000 per QALY, and the ICER of infliximab versus etanercept is ~£76,000 per QALY. Adalimumab is extendedly dominated in this group.

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Sensitivity analysis (AIC)

- Series of sensitivity analysis. Results sensitive to:
  - Length of treatment effect for biologics (10 years rather than 40 years).
  - Assumptions about the prescription cost.
  - Cost of treating patients who do not achieve a response to biologics for the psoriasis component of PsA.
  - Assumptions about the progression of HAQ on and off treatment.

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Conclusions

- Under base-case assumptions, etanercept would be considered the most cost-effective strategy for patients with PsA and minimal, mild-to-moderate or moderate-to-severe psoriasis.
- Etanercept appeared most likely to be cost-effective for patients with PsA and mild-to-moderate psoriasis who have failed adalimumab or infliximab as first-line therapy.
- For patients with PsA and mild-to-moderate psoriasis who have failed etanercept as first-line therapy, adalimumab seems most likely to be cost-effective at a threshold of £20,000 per QALY, though infliximab is most likely to be cost-effective if the threshold is £30,000 per QALY.

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Limitations & outstanding uncertainties

- Bayesian indirect comparison analyses provide evidence of the relative efficacy of these biologics; however, those findings may be considered more uncertain than would be provided in head-to head RCTs.
- The patients in most trials are not precisely representative of the population recommended for biologics in current guidelines. It is unclear whether the beneficial effects are similar in those treated in routine clinical practice.
- The adverse event data are derived primarily from patients with RA or other indications. The generalisability of these findings to PsA patients remains unclear.

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Limitations & outstanding uncertainties (2)

- The progression of HAQ on and off treatment, and the length of time over which biologics are assumed to be effective.
- The long term progression of PsA with and without biologics.
- The relationship between utility and severity of arthritis and psoriasis.
- Alternative rules about continuing therapy beyond 3 months depending on response.
- The health care costs of treating psoriasis of varying severity.